IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Group Art Unit 1612

In re Patent Application of

Simon Michael West et al.

Serial No. 10/551,203

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"ALKALOID FORMULATIONS"

Electronically filed with the United States Patent and Trademark Office by:

Sally Sorensen

Date: June 19, 2009

**DECLARATION OF SIMON MICHAEL WEST UNDER 37 C.F.R. § 1.132**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Simon Michael West, do hereby declare and state the following:

1. I am currently a Chief Scientist of Phosphagenics Limited, and a Director of Vital Health Sciences Pty Ltd.
2. I received a Dipolma of Applied Chemistry and a Bachelor of Science (double major in chemistry), University of Western Australia, as well as a Doctorate of Applied Science (Hons), RMIT University.
3. I am a co-inventor of the subject matter of all claims pending in the above-identified patent application. I make this declaration in support of prosecution of the subject application before the U.S. Patent and Trademark Office ("USPTO").
4. I have read and understood the invention as disclosed in the above-identified patent application, including the invention described by the presently pending claims.
5. I have reviewed the Office Action of December 19, 2008. I understand that claims 1-4, 6-7, 9-18, and 21-25 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,444,234 to Kirby et al. ("Kirby"), in view of WO 02/40033 to Tocovite Pty Ltd. ("Tocovite"), and further in view of U.S. Patent Pub. 2003/0157326 to Vaghefi et al. ("Vaghefi").
6. I am the sole inventor of Tocovite and conceived of all the subject matter disclosed therein.

7. As discussed in Tocovite, the use of free tocopherol had been avoided because it is unstable, and therefore suitable derivatives were sought. Tocovite at page 2, lines 10-11. Accordingly, in developing the invention disclosed in Tocovite, I found that the "use of a non-purified or semi-purified electron transfer agent phosphorylation therapeutic product is efficacious." Tocovite at page 3, lines 2-3. "In particular, the non-water soluble di-electron transfer agent phosphate derivatives do not have a deleterious effect on the efficacy of the therapeutic product and may even provide a synergistic effect which results in beneficial properties which enhance the dermal penetration and/or efficacy of the mono-electron agent phosphate derivatives." Tocovite at page 3, lines 3-7. Accordingly, Tocovite discloses an emulsion composition comprising a particular equimolar amount of a mono-electron transfer agent phosphate derivative (e.g., mono-tocopheryl phosphate), a di-electron transfer agent phosphate derivative (e.g., di-tocopheryl phosphate), and a suitable carrier. Abstract. In short, my work in Tocovite was focused on enhancing the dermal penetration and/or efficacy of mono-electron transfer agent phosphate derivatives.

8. Tocovite discloses compositions that enhance the dermal penetration and/or efficacy of mono-electron transfer agent phosphate derivatives. In my opinion, the disclosure in Tocovite would not motivate one of skill in the art to include alkaloids in those formulations, although the use of alkaloids would not be precluded. Again, my focus in developing Tocovite was on enhancing the dermal penetration and/or efficacy of mono-electron transfer agent phosphate derivatives.

9. Kirby discloses pharmaceutical compositions for the transdermal administration of a medicament, or other active agent, by topical application of the composition to the skin of humans. Abstract. The pharmaceutical compositions are based on a transdermal delivery system (TDS) wherein the medicament is modified to form a true solution in a complex formed from particular solvents and solvent and solute modifiers in combination with skin stabilizers. Abstract. Kirby is directed to topical formulations comprising (1) an active agent; (2) a solvent system in which the active is agent is soluble; and (3) a substance capable of *in vivo* stimulation of 3',5'-cyclic adenosine monophosphate (CAMP) or 3',5'-cyclic guanosine monophosphate (CGMP). Kirby, col. 6, ln 21-26.

10. The formulations of Kirby may apply the same general chemistry of association, in that a weak complex is formed between the active agent and its other components. However, Kirby follows the practice of transdermal transport based on the careful studies of the migration of a wide variety of molecules through the skin. This theory excludes sulfate and phosphate derivatives because they were not considered to efficiently transfer through the skin and thus would not have been considered appropriate or suitable for such formulations.

11. Against this background, we were initially reluctant to use sulfate or phosphate derivatives of hydrophobic substrates, such as tocopheryl phosphates, to activate the transdermal delivery of active agents, such as alkaloids. We had thought however that such class of derivatives might be unique because they are so important for human metabolism. In addition, we considered that there might be some unusual activity uniquely associated with these highly conserved compounds. Understandably, we were surprised when high levels of transdermal transport were demonstrated with alkaloids.

12. Accordingly, in my opinion, Tocovite would not have suggested modifying the formulations of Kirby to arrive at the claimed invention. In particular, one of skill in the art would not have been motivated by Tocovite to 1) phosphorylate the solvent modifiers of Kirby, 2) use water as a solvent, rather than the ethanol/propylene glycol solvent of Kirby, or 3) remove the forskolin of Kirby.

13. Furthermore, in my opinion, phosphorylating Kirby's solvent modifiers, e.g., lemon oil (or/and d-limonene), Vitamin E, Pro-Vitamin B, D-panthenol and methylsulfonylmethane (MSM), (Kirby col. 11, lns. 11-14) would not achieve the efficacy of the claimed alkaloid formulations. This is because the Stock Delivery System of Kirby is highly unsuitable for use with sulfate or phosphate derivatives of hydrophobic substrates.

14. Vaghefi teaches pharmaceutical compositions comprising microspheres with a water insoluble organic matrix in an interior region, throughout which are dispersed a plurality of microcapsules containing hydrophobic bioactive compounds. Abstract. The microcapsules located in the interior of the microspheres are coated with pharmaceutically-acceptable, charged (hyrdophilic) materials, thereby facilitating the transport of the hydrophobic bioreactive compounds. See Abstract, paragraphs [0014] to [0019].

15. In my opinion, those skilled in the art, considering Vaghefi in light of Tocovite, Kirby, or both, would simply dismiss Vaghefi because Vaghefi requires elaborate microsphere structures to assure that hydrophobic compounds can be transported across the dermal boundary. Vaghefi at [0014] to [0017]. The microspheres of Vaghefi are prepared by a process comprising spraying, into a chilling zone, a flowable dispersion of bioactive micron sized organic particles containing charged organic moieties in a water insoluble fluid matrix, under conditions that form droplets of said dispersion, and maintaining the fluidity of, and charge on, said droplets for a time sufficient to distribute homogenously said particles within said droplets, and solidifying said droplets into said microspheres. Vaghefi at [0015]. The particles are then incorporated in pharmaceutical compositions. Vaghefi at [0016]. Therefore, contrary to the Examiner's assertion that Vaghefi stands for and would provide motivation for using tocopherol phosphate as a bio enhancer, it is my opinion that one skilled in the art would instead glean from Vaghefi an elaborate system

that is much different from, and not compatible with, Tocovite or Kirby. As such, Vaghefi would be readily dismissed.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 15 June 2009

Simon Michael West